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SNELL & WILMER
ONE ARIZONA CENTER
400 EAST VAN BUREN
PHOENIX, AZ 85004-2202

EXAMINER
COUNTS, GARY W

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 12/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/808,275

Applicant(s)

NELSON ET AL.

Examiner

Gary W. Counts

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 September 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 31-48 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 31-48 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____

DETAILED ACTION

Status of the claims

The amendment filed September 20, 2004 is acknowledged and has been entered.

Double Patenting

Claims 31, 36 and 41 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of copending Application No. 09/808314. Although the conflicting claims are not identical, they are not patentably distinct from each other because it would have been obvious to one of ordinary skill in the art to determine and identify the analyte by using mass spectrometry for molecular weight analysis.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

Claims 32, and 36-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 32, part (b), is vague and indefinite because the recitation "post-combination affinity reagent; and". There is no recitation following the and, therefore it is unclear if applicant intends the claim to further include something else. It appears the claim has been abruptly ended without concluding its intended purpose. Please clarify.

Claim 36 is vague and indefinite because it is unclear if a single type of antibody binds to different types of species (i.e. does the same antibody bind to species A, B, and C) or are there different types of antibodies specific for different types of species (i.e. antibody A binds species A and antibody B binds species B). The specification on page 19 discloses that antibodies to each antigen to be detected are immobilized on a solid substrate creating the affinity reagent. Appropriate claim correction is required. Applicant is cautioned not to introduce new matter in the event of amendment to the claim.

Claim 45 the recitation "the mass spectrometric mixture" there is insufficient antecedent basis for this limitation.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

2. Claims 31, 32, 34 and 45 are rejected under 35 U.S.C. 102(a) as being anticipated by Papac et al., Direct Analysis of Affinity-Bound Analytes by MALDI/TOF MS, Anal. Chem.. 1994, 66, 2609-2613).

Papac et al disclose a method for the Mass spectral identification and detection of analytes separated by immunoaffinity chromatography (abstract). Papac et al disclose antibody immobilized to agarose beads and used as affinity columns (p. 2611). Papac et al disclose passing a solution of horse heart cytochrome c (physiological

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specimen) through the column. Papac et al teaches that the immobilized antibody captures the cytochrome c (post-combination affinity reagent) (p. 2611). Papac et al disclose washing to remove any unbound cytochrome c. Papac et al disclose that the sample is mixed with the beads and centrifuged and supernatant removed. Papac et al discloses that a matrix containing formic acid was added and the supernatant was tested by mass spectrometry (p. 2611, col 1 & p. 2613, col 2). Papac et al disclose that the captured analyte was released (eluted).

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 33 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Papac et al (Anal. Chem.) in view of Rampal et al (US 5,437,979).

See above for teachings of Papace et al (Anal. Chem.).

Papac et al (Anal Chem.) differs from the instant invention in failing to teach combining the affinity reagent with the specimen using a micropipette tip in which there is a filter element which retains the affinity reagent.

Rampal et al disclose a micropipette tip in which solid substrates are retained by porous frits (filter element). Rampal et al disclose that these solid substrates comprise immobilized reactants, which bind to an analyte of interest. Rampal et al disclose that the use of the micropipette tips in this manner minimizes exposure of the solid phase to the surroundings by retaining the solid phase in an almost fully enclosed environment, thereby enhancing reliability, reproducibility and safety (col 1, lines 35-50).

It would have been obvious to one of ordinary skill in the art to incorporate the beads of Papac et al into a micropipette such as taught by Rampal et al because Rampal et al discloses that these pipette tips can be used in reaction assays and also minimizes exposure of the solid phase to the surroundings by retaining the solid phase in an almost fully enclosed environment, thereby enhancing reliability, reproducibility and safety.

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7. Claims 36, 37, 39 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Papac et al (Anal Chem.) in view of Awata et al (Immunoaffinity Extraction of 4-Hydroxy-2-(4-methylphenyl)benzothiazole and Its Metabolites for Determination by Gas chromatography-Mass Spectrometry, Biol. Pharm. Bull. 17(6) 843-845 (1994)).

See above for teachings of Papac et al (Anal. Chem.).

Papac et al differ from the instant invention in failing to teach the affinity reagent having a specific affinity for more than one analyte species.

Awata et al disclose antibodies which have a broad spectrum of affinity, not only for an analyte of interest but also for metabolites of the analyte (abstract & p. 843). Awata et al disclose that this type of antibody provides for the simultaneous extraction of related substances and for their simultaneous determination.

It would have been obvious to one of ordinary skill in the art to incorporate antibodies as taught by Awata et al into the method of Papac et al. (Anal Chem.) because Awata et al shows that this type of antibody provides for the simultaneous extraction of related substances and for their simultaneous determination and further because Papac teaches the determination of analytes and that immunoaffinity separation and purification techniques based upon these methodologies are of increasing importance in biotechnology (p. 2609).

With respect to the recitation "wherein the affinity reagent includes more than one antibody immobilized onto a solid substrate" as recited in the instant claims. One of ordinary skill would recognize that the solid substrate (bead) of Papac et al would

comprises more than a single antibody in order to function properly. Further, as stated above it is unclear if a single type of antibody binds to different types of species (i.e. does the same antibody bind to species A, B, and C) or are there different types of antibodies specific for different types of species (i.e. antibody A binds species A and antibody B binds species B). Therefore, the combination of Papac et al and Atawa et al reads on the instantly recited claims.

8. Claims 38 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Papac et al (Anal. Chem.) and Awata et al. in view of Rampal et al (US 5,437,979).

See above for teachings of Papac et al (Anal. Chem.) and Awata et al.

Papac et al (Anal Chem.) and Atawa et al differ from the instant invention in failing to teach combining the affinity reagent with the specimen using a micropipette tip in which there is a filter element which retains the affinity reagent.

Rampal et al disclose a micropipette tip in which solid substrates are retained by porous frits (filter element). Rampal et al disclose that these solid substrates comprise immobilized reactants, which bind to an analyte of interest. Rampal et al disclose that the use of the micropipette tips in this manner minimizes exposure of the solid phase to the surroundings by retaining the solid phase in an almost fully enclosed environment, thereby enhancing reliability, reproducibility and safety (col 1, lines 35-50).

It would have been obvious to one of ordinary skill in the art to incorporate the modified beads of Papac et al into a micropipette such as taught by Rampal et al because Rampal et al discloses that these pipette tips can be used in reaction assays and also minimizes exposure of the solid phase to the surroundings by retaining the

solid phase in an almost fully enclosed environment, thereby enhancing reliability, reproducibility and safety.

9. Claims 41 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Papac et al (Anal Chem.) and Awata et al in view of Mackert et al (Journ. Of Chromatography, 494 (1989) 13-22) or Chiabrando et al (Journ of Chromatography 495 (1989) 1-11).

See above for teachings of Papac et al and Awata et al.

Papac et al and Awata et al differ from the instant invention in failing to specifically teach a plurality of different antibodies each specific to a different analyte species.

Mackert et al and Chiabrando et al teach immobilizing a plurality of different antibodies to capture and isolate different analytes.

It would have been obvious to one of ordinary skill in the art to incorporate a plurality of different antibodies as taught by Mackert et al or Chiabrando et al into the modified method of Papac et al because Awata et al specifically teaches that it is known in the art to co-immobilize several characteristic antibodies and Awata et al specifically refers to the Mackert et al and Chiabrando et al references (p. 843, first paragraph) and therefore, one of ordinary skill in the art would have a reasonable expectation of success incorporating co-immobilized different antibodies for separating and detection analytes of interest.

10. Claim 42, 43 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Papac et al and Awata et al in view of Mackert et al or Chiabrando et al as applied to claims 36, 37, 39 and 41 above, and further in view of Rampal et al (US 5,437,979).

See above for teachings of Papac et al (Anal. Chem.), Awata et al., Mackert et al and Chiabrando et al.

Papac et al (Anal Chem.) Atawa et al., Mackert et al and Chiabrando et al differ from the instant invention in failing to teach combining the affinity reagent with the specimen using a micropipette tip in which there is a filter element which retains the affinity reagent.

Rampal et al disclose a micropipette tip in which solid substrates are retained by porous frits (filter element). Rampal et al disclose that these solid substrates comprise immobilized reactants, which bind to an analyte of interest. Rampal et al disclose that the use of the micropipette tips in this manner minimizes exposure of the solid phase to the surroundings by retaining the solid phase in an almost fully enclosed environment, thereby enhancing reliability, reproducibility and safety (col 1, lines 35-50).

It would have been obvious to one of ordinary skill in the art to incorporate the modified beads of Papac et al into a micropipette such as taught by Rampal et al because Rampal et al discloses that these pipette tips can be used in reaction assays and also minimizes exposure of the solid phase to the surroundings by retaining the solid phase in an almost fully enclosed environment, thereby enhancing reliability, reproducibility and safety.

11. Claim 48 is rejected under 35 U.S.C. 103(a) as being unpatentable over Papac et al (Anal. Chem.) in view of Williams et al (US 5,135,870).

See above for teachings of Papac et al.

Papac et al differ from the instant invention in failing to specifically teach adding a laser desorption/ionization agent to the released and isolated analyte species to form a mass spectrometric mixture.

Williams et al disclose that prior to analysis by mass spectrometry a sample should be volatilized in a liquid or solid matrix (col 1). Williams et al teaches this provides for the mass spectrometric analysis of proteins without fragmentation or degradation, or with controlled fragmentation.

It would have been obvious to one of ordinary skill in the art to incorporate a matrix as taught by Williams et al with the supernatant containing the analyte of Papac et al because Williams et al shows that this provides for the mass spectrometric analysis of proteins without fragmentation or degradation, or with controlled fragmentation.

Response to Arguments

12. Applicant's arguments with respect to claims 31-47 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

13. No claims are allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Gary Counts
Examiner
Art Unit 1641
November 17, 2004



LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

11/24/04